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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation

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 NEWS 42   Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43   Jun 06  PASCAL enhanced with additional data
 NEWS 44   Jun 20  2003 edition of the FSTA Thesaurus is now available
 NEWS 45   Jun 25  HSDB has been reloaded

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 12:26:58 ON 02 JUL 2003

=> FIL MEDLINE BIOSIS EMBASE CA SCISEARCH
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     1.05       1.05

FILE 'MEDLINE' ENTERED AT 12:29:43 ON 02 JUL 2003

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FILE 'CA' ENTERED AT 12:29:43 ON 02 JUL 2003
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FILE 'SCISEARCH' ENTERED AT 12:29:43 ON 02 JUL 2003
COPYRIGHT 2003 THOMSON ISI

=> s ribozym
=> s ribozym?
L1       20453 RIBOZYM?

=> s hiv?
L2      579600 HIV?

=> s l1 and l2
L3         1603 L1 AND L2

=> s l3 and py<1994
   2 FILES SEARCHED...
L4          253 L3 AND PY<1994

=> s l4 and (l1 (5n) (conjug? or bind? or bound?) (5n) ((3!utr or 3!!utr) or
((pack? or dimer?) (3n)  sign?)))
```

```
   3 FILES SEARCHED...
TERM '3!!UTR' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED
L5          0 L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?) (5N) ((3!UTR OR
              3!!UTR) OR ((PACK? OR DIMER?) (3N) SIGN?)))
You have entered a truncated stem which occurs in too many terms.
Make the stem longer and try again.  For example, if your original
term was 'degr?' to search for variations and the abbreviation for
'degradation', you could replace it with the expression '(degrdn OR
degrad?)'.  If your search term was numeric, e.g., 'C>5', reduce the
size of the range.

=> s l4 and (l1 (5n) (conjug? or bind? or bound?))
L6          8 L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?))

=> dup rem 6
ENTER L# LIST OR (END):16
'6' IS NOT VALID.  VALID FILE NAMES ARE 'MEDLINE, BIOSIS, CA, SCISEARCH'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7           5 DUP REM L6 (3 DUPLICATES REMOVED)

=> d l7 1-7 ibib abs

L7   ANSWER 1 OF 5  CA  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        120:290083  CA
TITLE:                   Chimeric tRNALYS-ribozyme molecules, and use
                         for inhibition of human immunodeficiency virus 1
INVENTOR(S):             Rossi, John J.; Larson, Garry P.
PATENT ASSIGNEE(S):      City of Hope, USA
SOURCE:                  PCT Int. Appl., 15 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  3
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
     WO 9324133         A1   19931209      WO 1992-US4362    19920527 <--
         W:  AU, CA, JP, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
     AU 9221694         A1   19931230      AU 1992-21694     19920527 <--
     AU 674656          B2   19970109
     EP 596901          A1   19940518      EP 1992-913946    19920527
     EP 596901          B1   20000809
         R:  DE, FR, GB
     US 5827935         A    19981027      US 1994-185827    19940124
PRIORITY APPLN. INFO.:                  WO 1992-US4362   A  19920527
AB   The invention provides novel chimeric tRNALYS-ribozyme mols.
     that compete effectively with tRNALYS for HIV-1 reverse
     transcriptase binding sites.  The chimeric human tRNALYS-ribozymes
     inhibit reverse HIV transcription by delivering inhibitors such
     as ribozymes of HIV-1 reverse transcriptase directly
     to the virion particle and render it nonfunctional.  The chimeric mols. of
     the invention thus serve as highly specific nontoxic therapeutic agents.
     Also presented is a demonstration of RNase activity of HIV-1
     reverse transcriptase when tRNALYS-ribozyme and HIV-1
     primer binding site transcripts are incubated together in the
```

presence of **HIV**-1 reverse transcriptase. The structure of one chimeric tRNALYS-**ribozyme** is included.

L7 ANSWER 2 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 94043296 MEDLINE
DOCUMENT NUMBER: 94043296 PubMed ID: 8227004
TITLE: Optimization of an anti-**HIV** hairpin **ribozyme** by in vitro selection.
AUTHOR: Joseph S; Burke J M
CORPORATE SOURCE: Department of Microbiology and Molecular Genetics, Markey Center for Molecular Genetics, University of Vermont, Burlington 05405.
CONTRACT NUMBER: AI29892 (NIAID)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, **(1993 Nov 25)** 268 (33) 24515-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931220

AB We have applied in vitro selection methods to achieve a large increase in the catalytic activity of a hairpin **ribozyme** targeted against a highly conserved 14-nucleotide sequence within **HIV**-1 pol RNA. The substrate specificity was changed by mutating 8 bases within the substrate-**binding** domain of the parental (-)sTRSV **ribozyme**. The resulting enzyme cleaved the **HIV** substrate specifically but with a 20-fold reduction in catalytic efficiency (kcat/KM). Following random mutagenesis, **ribozymes** with increased activity against the target sequence were selected through 10 rounds of in vitro selection. Selective pressure was increased by decreasing MgCl2 and spermidine concentrations, and reducing reaction time. Variant **ribozymes** with base substitutions A11-->G and U39-->C were selected in the population. These mutations were introduced singly and in combination into the trans-acting anti-**HIV** **ribozyme**. Each of the single-base substitutions significantly increased **ribozyme** activity, while the activity of double mutant was increased to nearly the level of the parental **ribozyme**. These findings demonstrate that in vitro selection is a powerful and efficient method to optimize **ribozymes** for the catalytic inactivation of targeted RNA molecules.

L7 ANSWER 3 OF 5 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 120:131451 CA
TITLE: Gene therapy for AIDS
AUTHOR(S): Nagayama, Hitomi; Tani, Kenzaburo
CORPORATE SOURCE: Inst. Med. Sci., Univ. Tokyo, Tokyo, 108, Japan
SOURCE: Molecular Medicine (Tokyo, Japan) (**1993**), 30(12), 1558-60
CODEN: MOLMEL; ISSN: 0918-6557
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review, with 8 refs., on the results and problems to be solved in gene therapy of **HIV** infection; antisense method, RNA decoy using TAR (tat **binding** motif), **ribozyme** cutting gag RNA or 5' leader sequence, mutant gene methods using dominant neg. effects on rev gene, and triple-helix formation method. Gene therapy using env gene is involved in cellular immunity.

L7 ANSWER 4 OF 5 CA COPYRIGHT 2003 ACS

ACCESSION NUMBER: 118:33950 CA
TITLE: Conjugates of a glycoprotein with a nucleic acid-binding substance to induce cell transfection in gene therapy
INVENTOR(S): Birnstiel, Max L.; Cotten, Matthew; Wagner, Ernst
PATENT ASSIGNEE(S): Genentech, Inc., USA; Boehringer Ingelheim International G.m.b.H.
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 4115038	A1	19921112	DE 1991-4115038	19910508	<--
CA 2105771	AA	19921109	CA 1992-2105771	19920501	<--
WO 9219281	A2	19921112	WO 1992-EP953	19920501	<--
WO 9219281	A3	19930204			
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
EP 584118	A1	19940302	EP 1992-909423	19920501	
EP 584118	B1	20000927			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
JP 06507158	T2	19940811	JP 1992-508535	19920501	
JP 3351524	B2	20021125			
AT 196608	E	20001015	AT 1992-909423	19920501	
ES 2150421	T3	20001201	ES 1992-909423	19920501	

PRIORITY APPLN. INFO.: DE 1991-4115038 A 19910508
WO 1992-EP953 W 19920501

AB A glycoprotein (e.g. transferrin, **HIV** envelope glycoprotein gp120, or a monoclonal antibody to a cell surface protein) is attached to a nucleic acid-binding substance (preferably a homologous polycationic polypeptide, e.g. polylysine, histone, protamine, DNA-binding protein) by oxidizing the carbohydrate moiety of the glycoprotein to the aldehyde form and coupling the aldehyde groups to amino groups on the nucleic acid-binding substance. Nucleic acid bound by the conjugate is taken up by cells which express on their surface a protein which binds the glycoprotein. Thus, human transferrin was oxidized with NaIO4 and conjugated with poly-L-lysine and the product was reduced with NaBH3CN and complexed with Fe3+ and a plasmid contg. the luciferase gene from Photinus pyralis and a promoter. The complex was used to transfect K562 erythroleukemia cells via the transferrin receptor; the transfected cells expressed luciferase.

L7 ANSWER 5 OF 5 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 114:58155 CA
TITLE: Preparation of synthetic **ribozymes** derived from catalytic sequence of tobacco ringspot virus satellite RNA
INVENTOR(S): Hampel, Arnold E.; Tritz, Richard H.; Hicks, Margaret F.
PATENT ASSIGNEE(S): Northern Illinois University, USA; Biotechnology Research and Development Corp., Inc.
SOURCE: Eur. Pat. Appl., 53 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 360257	A2	19900328	EP 1989-117424	19890920	<--
EP 360257	A3	19910417			
EP 360257	B1	19961113			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 1340323	A1	19990119	CA 1989-611953	19890919	
AU 8941594	A1	19900329	AU 1989-41594	19890920	<--
AU 641900	B2	19931007			
JP 03123485	A2	19910527	JP 1989-244890	19890920	<--
JP 3167304	B2	20010521			
EP 700996	A1	19960313	EP 1995-115981	19890920	
EP 700996	B1	19971126			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AT 145239	E	19961115	AT 1989-117424	19890920	
ES 2095210	T3	19970216	ES 1989-117424	19890920	
AT 160584	E	19971215	AT 1995-115981	19890920	
EP 812912	A1	19971217	EP 1997-107205	19890920	
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
ES 2112006	T3	19980316	ES 1995-115981	19890920	
US 5866701	A	19990202	US 1993-78774	19930617	
AU 9344207	A1	19931202	AU 1993-44207	19930726	<--
AU 659330	B2	19950511			
US 5527895	A	19960618	US 1993-153367	19931116	
US 5856188	A	19990105	US 1995-485689	19950607	
US 5858785	A	19990112	US 1995-476021	19950607	
US 5869339	A	19990209	US 1995-478608	19950607	
US 6221661	B1	20010424	US 1995-476423	19950607	
AU 9528503	A1	19960328	AU 1995-28503	19950811	
AU 691007	B2	19980507			

PRIORITY APPLN. INFO.:

US 1988-247100	A	19880920
EP 1989-117424	A3	19890920
EP 1995-115981	A3	19890920
US 1989-409666	B2	19890920
US 1990-577658	B2	19900904
US 1991-703427	B1	19910514
US 1993-78774	A3	19930617
US 1993-153367	A3	19931116

AB A synthetic **ribozyme** (I) having a sequence similar to that of the catalytic center of the (-) sense strand of the tobacco ringspot virus satellite RNA (as derived by computer modeling) and its analogs are prepd. by in vitro transcription of chem. synthesized DNA templates. The **ribozymes** comprise a linear substrate-**binding** portion and a hairpin portion, and cleave their substrates 5' to the sequence GUC. Their catalytic action is different from that of other catalytic RNA's which fit the "hammerhead" model. I has a Km and Kcat for its substrate of 0.03 .mu.M and 2.1/min, resp. The effects of changing bases on the activity of I were studied. Analogs cleaving sequences within the **HIV**-1 genome and chloramphenicol acetyl transferase mRNA were also prepd.

=> d his

(FILE 'HOME' ENTERED AT 12:26:58 ON 02 JUL 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 12:29:43 ON 02 JUL 2003

L1 20453 S RIBOZYM?
L2 579600 S HIV?
L3 1603 S L1 AND L2
L4 253 S L3 AND PY<1994
L5 0 S L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?) (5N) ((3!UTR OR
L6 8 S L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?))

L7 5 DUP REM L6 (3 DUPLICATES REMOVED)

=> d l6 7-8 ibib abs

L6 ANSWER 7 OF 8 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 114:58155 CA
TITLE: Preparation of synthetic **ribozymes** derived from catalytic sequence of tobacco ringspot virus satellite RNA
INVENTOR(S): Hampel, Arnold E.; Tritz, Richard H.; Hicks, Margaret F.
PATENT ASSIGNEE(S): Northern Illinois University, USA; Biotechnology Research and Development Corp., Inc.
SOURCE: Eur. Pat. Appl., 53 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 360257	A2	19900328	EP 1989-117424	19890920	<--
EP 360257	A3	19910417			
EP 360257	B1	19961113			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 1340323	A1	19990119	CA 1989-611953	19890919	
AU 8941594	A1	19900329	AU 1989-41594	19890920	<--
AU 641900	B2	19931007			
JP 03123485	A2	19910527	JP 1989-244890	19890920	<--
JP 3167304	B2	20010521			
EP 700996	A1	19960313	EP 1995-115981	19890920	
EP 700996	B1	19971126			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
AT 145239	E	19961115	AT 1989-117424	19890920	
ES 2095210	T3	19970216	ES 1989-117424	19890920	
AT 160584	E	19971215	AT 1995-115981	19890920	
EP 812912	A1	19971217	EP 1997-107205	19890920	
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
ES 2112006	T3	19980316	ES 1995-115981	19890920	
US 5866701	A	19990202	US 1993-78774	19930617	
AU 9344207	A1	19931202	AU 1993-44207	19930726	<--
AU 659330	B2	19950511			
US 5527895	A	19960618	US 1993-153367	19931116	
US 5856188	A	19990105	US 1995-485689	19950607	
US 5858785	A	19990112	US 1995-476021	19950607	
US 5869339	A	19990209	US 1995-478608	19950607	
US 6221661	B1	20010424	US 1995-476423	19950607	
AU 9528503	A1	19960328	AU 1995-28503	19950811	
AU 691007	B2	19980507			

PRIORITY APPLN. INFO.:
US 1988-247100 A 19880920
EP 1989-117424 A3 19890920
EP 1995-115981 A3 19890920
US 1989-409666 B2 19890920
US 1990-577658 B2 19900904
US 1991-703427 B1 19910514
US 1993-78774 A3 19930617
US 1993-153367 A3 19931116

AB A synthetic **ribozyme** (I) having a sequence similar to that of the catalytic center of the (-) sense strand of the tobacco ringspot virus satellite RNA (as derived by computer modeling) and its analogs are prepd. by in vitro transcription of chem. synthesized DNA templates. The **ribozymes** comprise a linear substrate-**binding** portion

and a hairpin portion, and cleave their substrates 5' to the sequence GUC. Their catalytic action is different from that of other catalytic RNA's which fit the "hammerhead" model. I has a Km and Kcat for its substrate of 0.03 .mu.M and 2.1/min, resp. The effects of changing bases on the activity of I were studied. Analogs cleaving sequences within the **HIV**-1 genome and chloramphenicol acetyl transferase mRNA were also prepd.

L6 ANSWER 8 OF 8 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 93:689661 SCISEARCH
THE GENUINE ARTICLE: MG673
TITLE: OPTIMIZATION OF AN ANTI-**HIV** HAIRPIN **RIBOZYME** BY IN-VITRO SELECTION
AUTHOR: JOSEPH S; BURKE J M (Reprint)
CORPORATE SOURCE: UNIV VERMONT, MARKEY CTR MOLEC GENET, DEPT MICROBIOL & MOLEC GENET, STAFFORD HALL, BURLINGTON, VT, 05405
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (**25 NOV 1993**) Vol. 268, No. 33, pp. 24515-24518. ISSN: 0021-9258.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 27

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have applied in vitro selection methods to achieve a large increase in the catalytic activity of a hairpin **ribozyme** targeted against a highly conserved 14-nucleotide sequence within **HIV**-1 pol RNA. The substrate specificity was changed by mutating 8 bases within the substrate-**binding** domain of the parental (-)sTRSV **ribozyme**. The resulting enzyme cleaved the **HIV** substrate specifically but with a 20-fold reduction in catalytic efficiency (k(cat)/K(M)). Following random mutagenesis, **ribozymes** with increased activity against the target sequence were selected through 10 rounds of in vitro selection. Selective pressure was increased by decreasing MgCl2 and spermidine concentrations, and reducing reaction time. Variant **ribozymes** with base substitutions A11 --> G and U39 --> C were selected in the population. These mutations were introduced singly and in combination into the trans-acting anti-**HIV** **ribozyme**. Each of the single-base substitutions significantly increased **ribozyme** activity, while the activity of double mutant was increased to nearly the level of the parental **ribozyme**. These findings demonstrate that in vitro selection is a powerful and efficient method to optimize **ribozymes** for the catalytic inactivation of targeted RNA molecules.

=> d his

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FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 12:29:43 ON 02 JUL 2003

L1 20453 S RIBOZYM?
L2 579600 S HIV?
L3 1603 S L1 AND L2
L4 253 S L3 AND PY<1994
L5 0 S L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?) (5N) ((3!UTR OR
L6 8 S L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?))
L7 5 DUP REM L6 (3 DUPLICATES REMOVED)

=> s l4 and (local? or position?)
L8 9 L4 AND (LOCAL? OR POSITION?)

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 4 DUP REM L8 (5 DUPLICATES REMOVED)

=> d l9 1-4 ibib abs

L9 ANSWER 1 OF 4 CA COPYRIGHT 2003 ACS
ACCESSION NUMBER: 119:154902 CA
TITLE: Enhancement of **ribozyme** catalytic activity by a neighboring facilitator oligonucleotide
INVENTOR(S): Goodchild, John
PATENT ASSIGNEE(S): Worcester Foundation for Experimental Biology, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9315194	A1	19930805	WO 1993-US783	19930204	<--
W: AU, CA, JP, KR, US					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9335977	A1	19930901	AU 1993-35977	19930204	<--
AU 661124	B2	19950713			
EP 625194	A1	19941123	EP 1993-904711	19930204	
EP 625194	B1	19960424			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07508638	T2	19950928	JP 1993-513431	19930204	
AT 137263	E	19960515	AT 1993-904711	19930204	
ES 2085767	T3	19960601	ES 1993-904711	19930204	
PRIORITY APPLN. INFO.:			US 1992-830713	A2 19920204	
			WO 1993-US783	A 19930204	

AB The rate of cleavage of target RNA by **ribozyme** is increased by providing an oligonucleotide which hybridizes to the target RNA at a distance .ltoreq.5 nucleotides from the site of **ribozyme** hybridization. This facilitator oligonucleotide also decreases the concn. of Mg2+ or Mn2+ needed in the reaction. This concept was demonstrated by **ribozymes** specific for **HIV**-1 RNA. The effects of **ribozyme** length, facilitator length and compn. (e.g., contg. ribo- or deoxyribonucleotides, oligos with altered phosphate backbones), and **position** of facilitator interaction with substrate RNA were examd.

L9 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 93324322 MEDLINE
DOCUMENT NUMBER: 93324322 PubMed ID: 8332458
TITLE: Nuclease-resistant chimeric **ribozymes** containing deoxyribonucleotides and phosphorothioate linkages.
AUTHOR: Shimayama T; Nishikawa F; Nishikawa S; Taira K
CORPORATE SOURCE: National Institute of Bioscience and Human Technology, Agency of Industrial Science & Technology, MITI, Tsukuba Science City, Japan.
SOURCE: NUCLEIC ACIDS RESEARCH, **(1993 Jun 11)** 21 (11) 2605-11.
Journal code: 0411011. ISSN: 0305-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930826

Last Updated on STN: 19970203
Entered Medline: 19930813

AB Hammerhead **ribozymes** are considered to be potential therapeutic agents for **HIV** virus because of their site-specific RNA cleavage activities. In order to elucidate structure--function relationship and also to hopefully endow **ribozymes** with resistance to ribonucleases, we firstly synthesized chimeric DNA/RNA **ribozymes** in which deoxyribonucleotides were substituted for ribonucleotides at noncatalytic residues (stems I, II, and III). Kinetic analysis revealed that (i) DNA in the hybridizing arms (stems I and III) enhanced the chemical cleavage step. (ii) stem II and its loop do not affect its enzymatic activity. Secondly, we introduced deoxyribonucleotides with phosphorothioate linkages to the same regions (stems I, II, and III) in order to test whether such thio-linkages further improve their resistance to nucleases. Kinetic measurements revealed that this chimeric thio-DNA/RNA **ribozyme** had seven-fold higher cleavage activity (kcat = 27 min-1) than that of the all-RNA **ribozyme**. In terms of stability in serum, DNA-armed **ribozymes** gained about 10-fold higher stability in human serum but no increase in stability was recognized in bovine serum, probably because the latter serum mainly contained endoribonucleases that attacked unmodified catalytic-loop regions of these **ribozymes**. Thirdly, in order to protect them from endoribonucleases, three additional modifications were made at **positions** U7, U4 and C3 within the internal catalytic-loop region, that succeeded in gaining more than a hundred times greater resistance to nucleases in both serums. More importantly, these catalytic-loop modified **ribozymes** had the comparable cleavage activity (kcat) to the wild-type **ribozyme**. Since these chimeric thio-DNA/RNA **ribozymes** are more resistant to attack by both exonucleases and endoribonucleases than the wild-type all-RNA **ribozymes** in vivo and since their cleavage activities are not sacrificed, they appear to be better candidates than the wild type for antiviral therapeutic agents.

L9 ANSWER 3 OF 4 MEDLINE
ACCESSION NUMBER: 92338541 MEDLINE
DOCUMENT NUMBER: 92338541 PubMed ID: 1821650
TITLE: Exploring the use of antisense, enzymatic RNA molecules (**ribozymes**) as therapeutic agents.
AUTHOR: Rossi J J; Elkins D; Taylor N; Zaia J; Sullivan S; Deshler J O
CORPORATE SOURCE: Department of Molecular Genetics, Beckman Research Institute of the City of Hope, Duarte, CA 91010.
CONTRACT NUMBER: AI25959 (NIAID)
AI29329 (NIAID)
SOURCE: ANTISENSE RESEARCH AND DEVELOPMENT, **(1991 Fall)** 1 (3) 285-8. Ref: 10
Journal code: 9110698. ISSN: 1050-5261.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920911
Last Updated on STN: 19970203
Entered Medline: 19920825

AB Antisense catalytic RNAs that specifically base-pair with and cleave target RNA sequences have potential for use as therapeutic agents against viral as well as endogenous gene expression. With the ultimate goal of developing anti-human immunodeficiency virus type 1 (**HIV**-1) **ribozymes** for therapeutic use, we have been exploring ways to improve upon the functional activity of **ribozymes** in living

cells. This is being done by the systematic exploration of parameters that affect antisense, and hence **ribozyme**, function. These include target accessibility, stability of the catalyst, methods for delivery, and intracellular **localization** of the **ribozyme** . In addition, we have been examining the kinetic consequences of having extra, nontargeted sequences appended to the **ribozyme** flanking sequences. Perhaps the single most important consideration for **ribozyme** effectiveness in an intracellular environment is the accessibility of the target RNA for cleavage. By exploiting the mechanisms by which naturally occurring antisense RNAs interact with their target sequences, we hope to be able to address this problem of targeting and fully capitalize upon the potential of **ribozymes** as therapeutic agents.

L9 ANSWER 4 OF 4 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 93027431 MEDLINE
DOCUMENT NUMBER: 93027431 PubMed ID: 1841379
TITLE: Structure-function relationship of hammerhead **ribozymes** as probed by 2'-modifications.
AUTHOR: Pieken W A; Olsen D B; Aurup H; Williams D M; Heidenreich O; Benseler F; Eckstein F
CORPORATE SOURCE: Max-Planck-Institut fur Experimentelle Medizin, Gottingen, FRG.
SOURCE: NUCLEIC ACIDS SYMPOSIUM SERIES, **(1991)** (24) 51-3. Journal code: 8007206. ISSN: 0261-3166.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 19930122
Last Updated on STN: 19970203
Entered Medline: 19921125
AB Hammerhead **ribozymes** containing 2'-fluoro- or 2'-aminonucleotides were prepared by automated chemical synthesis. Incorporation of 2'-fluorouridines, 2'-fluorocytidines or 2'-aminouridines did not appreciably decrease catalytic activity. The presence of 2'-aminocytidines, however, reduced the activity about 20-fold. No catalytic activity could be measured for **ribozymes** in which all adenosines were replaced by the 2'-fluoro analogue in presence of MgCl2. No single **position** could be found responsible for this loss of activity. In an attempt to construct **ribozymes** to hydrolyse **HIV**-RNA in the 5'-LTR region several constructs were tested on synthetic substrate as well as on run-off transcripts of about 1000 nucleotides length.

=> dhis
DHIS IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

(FILE 'HOME' ENTERED AT 12:26:58 ON 02 JUL 2003)

FILE 'MEDLINE, BIOSIS, EMBASE, CA, SCISEARCH' ENTERED AT 12:29:43 ON 02 JUL 2003
L1 20453 S RIBOZYM?
L2 579600 S HIV?
L3 1603 S L1 AND L2
L4 253 S L3 AND PY<1994

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L5            0 S L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?) (5N) ((3!UTR OR
L6            8 S L4 AND (L1 (5N) (CONJUG? OR BIND? OR BOUND?))
L7            5 DUP REM L6 (3 DUPLICATES REMOVED)
L8            9 S L4 AND (LOCAL? OR POSITION?)
L9            4 DUP REM L8 (5 DUPLICATES REMOVED)

=> s l4 and (ribozym? (5n) (bind? or bound? or append? or includ? or attach? or
tether? or conjug? or ligat?)
UNMATCHED LEFT PARENTHESIS 'AND (RIBOZYM?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s l4 and (ribozym? (5n) (bind? or bound? or append? or includ? or attach? or
tether? or conjug? or ligat?))
L10          26 L4 AND (RIBOZYM? (5N) (BIND? OR BOUND? OR APPEND? OR INCLUD?
                OR ATTACH? OR TETHER? OR CONJUG? OR LIGAT?))

=> dup rem l10
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L11           11 DUP REM L10 (15 DUPLICATES REMOVED)

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L11  ANSWER 1 OF 11  CA  COPYRIGHT 2003 ACS
AN   120:290083  CA
TI   Chimeric tRNALYS-ribozyme molecules, and use for inhibition of
     human immunodeficiency virus 1
IN   Rossi, John J.; Larson, Garry P.
PA   City of Hope, USA
SO   PCT Int. Appl., 15 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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PI   WO 9324133         A1   19931209      WO 1992-US4362   19920527 <--
         W:  AU, CA, JP, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
     AU 9221694         A1   19931230      AU 1992-21694    19920527 <--
     AU 674656          B2   19970109
     EP 596901          A1   19940518      EP 1992-913946   19920527
     EP 596901          B1   20000809
         R:  DE, FR, GB
     US 5827935         A    19981027      US 1994-185827   19940124
PRAI WO 1992-US4362     A    19920527

L11  ANSWER 2 OF 11     MEDLINE                          DUPLICATE 1
AN   94043296     MEDLINE
DN   94043296   PubMed ID: 8227004
TI   Optimization of an anti-HIV hairpin ribozyme by in
     vitro selection.
AU   Joseph S; Burke J M
CS   Department of Microbiology and Molecular Genetics, Markey Center for
     Molecular Genetics, University of Vermont, Burlington 05405.
NC   AI29892 (NIAID)
SO   JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Nov 25) 268 (33) 24515-8.
     Journal code: 2985121R. ISSN: 0021-9258.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals; AIDS
EM   199312
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ED Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931220

L11 ANSWER 3 OF 11 MEDLINE DUPLICATE 2
AN 93317677 MEDLINE
DN 93317677 PubMed ID: 8327516
TI A hairpin **ribozyme** inhibits expression of diverse strains of human immunodeficiency virus type 1.
CM Erratum in: Proc Natl Acad Sci U S A 1993 Sep 1;90(17):8303
AU Yu M; Ojwang J; Yamada O; Hampel A; Rapapport J; Looney D; Wong-Staal F
CS Department of Medicine, University of California, San Diego, La Jolla 92093-0665.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1993 Jul 1)** 90 (13) 6340-4.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199308
ED Entered STN: 19930820
Last Updated on STN: 19970203
Entered Medline: 19930806

L11 ANSWER 4 OF 11 CA COPYRIGHT 2003 ACS
AN 120:131451 CA
TI Gene therapy for AIDS
AU Nagayama, Hitomi; Tani, Kenzaburo
CS Inst. Med. Sci., Univ. Tokyo, Tokyo, 108, Japan
SO Molecular Medicine (Tokyo, Japan) (**1993**), 30(12), 1558-60
CODEN: MOLMEL; ISSN: 0918-6557
DT Journal; General Review
LA Japanese

L11 ANSWER 5 OF 11 MEDLINE DUPLICATE 3
AN 93181192 MEDLINE
DN 93181192 PubMed ID: 8441628
TI Folding of DNA substrate-hairpin **ribozyme** domains: use of deoxy 4-thiouridine as an intrinsic photolabel.
AU Dos Santos D V; Vianna A L; Fourrey J L; Favre A
CS Groupe de Photobiologie Moleculaire, Institut Jacques Monod, CNRS Universite Paris VII, France.
SO NUCLEIC ACIDS RESEARCH, **(1993 Jan 25)** 21 (2) 201-7.
Journal code: 0411011. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199303
ED Entered STN: 19930416
Last Updated on STN: 19970203
Entered Medline: 19930331

L11 ANSWER 6 OF 11 CA COPYRIGHT 2003 ACS
AN 119:63020 CA
TI **Ribozyme** cleavage of human immunodeficiency virus 1 (**HIV** -1) RNA
IN Rossi, John J.; Cantin, Edouard M.; Zaia, John A.; Chang, Pairoj
PA City of Hope, USA
SO U.S., 11 pp.
CODEN: USXXAM
DT Patent

LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5144019	A	19920901	US 1989-369489	19890621 <--
	AU 9066160	A1	19920520	AU 1990-66160	19901019 <--
	AU 649975	B2	19940609		
	EP 506666	A1	19921007	EP 1990-915888	19901019 <--
	EP 506666	B1	19970716		
	R: DE, FR, GB				
	JP 05502580	T2	19930513	JP 1990-515050	19901019 <--
	US 6069007	A	20000530	US 1991-798128	19911126
	US 5272262	A	19931221	US 1992-854598	19920609 <--
PRAI	US 1989-369489	A2	19890621		
	US 1989-401613	B3	19890831		
	WO 1990-US6032	A	19901019		

L11 ANSWER 7 OF 11 CA COPYRIGHT 2003 ACS
AN 118:33950 CA
TI Conjugates of a glycoprotein with a nucleic acid-binding substance to induce cell transfection in gene therapy
IN Birnstiel, Max L.; Cotten, Matthew; Wagner, Ernst
PA Genentech, Inc., USA; Boehringer Ingelheim International G.m.b.H.
SO Ger. Offen., 16 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4115038	A1	19921112	DE 1991-4115038	19910508 <--
	CA 2105771	AA	19921109	CA 1992-2105771	19920501 <--
	WO 9219281	A2	19921112	WO 1992-EP953	19920501 <--
	WO 9219281	A3	19930204		
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	EP 584118	A1	19940302	EP 1992-909423	19920501
	EP 584118	B1	20000927		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
	JP 06507158	T2	19940811	JP 1992-508535	19920501
	JP 3351524	B2	20021125		
	AT 196608	E	20001015	AT 1992-909423	19920501
	ES 2150421	T3	20001201	ES 1992-909423	19920501
PRAI	DE 1991-4115038	A	19910508		
	WO 1992-EP953	W	19920501		

L11 ANSWER 8 OF 11 MEDLINE DUPLICATE 4
AN 93028565 MEDLINE
DN 93028565 PubMed ID: 1409715
TI Inhibition of human immunodeficiency virus type 1 replication in human T cells by retroviral-mediated gene transfer of a dominant-negative Rev trans-activator.
AU Bevec D; Dobrovnik M; Hauber J; Bohnlein E
CS Sandoz Research Institute, Vienna, Austria.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1992 Oct 15)** 89 (20) 9870-4.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199211
ED Entered STN: 19930122

Last Updated on STN: 19970203
Entered Medline: 19921117

L11 ANSWER 9 OF 11 MEDLINE
AN 92338541 MEDLINE
DN 92338541 PubMed ID: 1821650
TI Exploring the use of antisense, enzymatic RNA molecules (**ribozymes**) as therapeutic agents.
AU Rossi J J; Elkins D; Taylor N; Zaia J; Sullivan S; Deshler J O
CS Department of Molecular Genetics, Beckman Research Institute of the City of Hope, Duarte, CA 91010.
NC AI25959 (NIAID)
AI29329 (NIAID)
SO ANTISENSE RESEARCH AND DEVELOPMENT, **(1991 Fall)** 1 (3) 285-8.
Ref: 10
Journal code: 9110698. ISSN: 1050-5261.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; AIDS
EM 199208
ED Entered STN: 19920911
Last Updated on STN: 19970203
Entered Medline: 19920825

L11 ANSWER 10 OF 11 CA COPYRIGHT 2003 ACS
AN 114:58155 CA
TI Preparation of synthetic **ribozymes** derived from catalytic sequence of tobacco ringspot virus satellite RNA
IN Hampel, Arnold E.; Tritz, Richard H.; Hicks, Margaret F.
PA Northern Illinois University, USA; Biotechnology Research and Development Corp., Inc.
SO Eur. Pat. Appl., 53 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 360257	A2	19900328	EP 1989-117424	19890920	<--
	EP 360257	A3	19910417			
	EP 360257	B1	19961113			
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	CA 1340323	A1	19990119	CA 1989-611953	19890919	
	AU 8941594	A1	19900329	AU 1989-41594	19890920	<--
	AU 641900	B2	19931007			
	JP 03123485	A2	19910527	JP 1989-244890	19890920	<--
	JP 3167304	B2	20010521			
	EP 700996	A1	19960313	EP 1995-115981	19890920	
	EP 700996	B1	19971126			
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
	AT 145239	E	19961115	AT 1989-117424	19890920	
	ES 2095210	T3	19970216	ES 1989-117424	19890920	
	AT 160584	E	19971215	AT 1995-115981	19890920	
	EP 812912	A1	19971217	EP 1997-107205	19890920	
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	ES 2112006	T3	19980316	ES 1995-115981	19890920	
	US 5866701	A	19990202	US 1993-78774	19930617	
	AU 9344207	A1	19931202	AU 1993-44207	19930726	<--
	AU 659330	B2	19950511			
	US 5527895	A	19960618	US 1993-153367	19931116	

	US 5856188	A	19990105	US 1995-485689	19950607
	US 5858785	A	19990112	US 1995-476021	19950607
	US 5869339	A	19990209	US 1995-478608	19950607
	US 6221661	B1	20010424	US 1995-476423	19950607
	AU 9528503	A1	19960328	AU 1995-28503	19950811
	AU 691007	B2	19980507		
PRAI	US 1988-247100	A	19880920		
	EP 1989-117424	A3	19890920		
	EP 1995-115981	A3	19890920		
	US 1989-409666	B2	19890920		
	US 1990-577658	B2	19900904		
	US 1991-703427	B1	19910514		
	US 1993-78774	A3	19930617		
	US 1993-153367	A3	19931116		

L11 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1993:52850 BIOSIS
DN PREV199395029152
TI Inhibition of human immunodeficiency virus type 1 replication in human T cells by retroviral-mediated gene transfer of a dominant-negative Rev trans-activator.
AU Bevec, Dorian; Dobrovnik, Marike; Hauber, Joachim; Boehnlein, Ernst (1)
CS (1) Sandoz Res. Inst., Brunnerstrasse 59, A-1235 Vienna Austria
SO Proceedings of the National Academy of Sciences of the United States of America, (1922) Vol. 89, No. 20, pp. 9870-9874.
ISSN: 0027-8424.
DT Article; Errata
LA English

=>

---Logging off of STN---

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	91.05	92.10

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.72	-3.72

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